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COCHLEAR PATHOLOGY IN PRESBYCUSIS

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A survey of the temporal bone collection at the Massachusetts Eye and Ear Infirmary reveals 21 cases that meet the criterion for the clinical diagnosis of presbycusis. It is evident that the previously advanced concept of four predominant pathologic types of presbycusis is valid, these being sensory, neural, strial, and cochlear conductive. An abrupt high-tone loss signals sensory presbycusis, a flat threshold pattern is indicative of strial presbycusis, and loss of word discrimination is characteristic of neural presbycusis. When the increments of threshold loss present a gradually decreasing linear distribution pattern on the audiometric scale and have no pathologic correlate, it is speculated that the hearing loss is caused by alterations in the physical characteristics of the cochlear duct, and the loss is identified as cochlear conductive presbycusis. It is clear that many individual cases do not separate into a specific type but have mixtures of these pathologic types and are termed mixed presbycusis. About 25% of all cases of presbycusis show none of the above characteristics and are classified as indeterminate presbycusis.

KEY WORDS — cochlear pathology, deafness of aging, presbycusis.

INTRODUCTION

Aging cochleae present disorders that are symmetric in paired ears; however, the extent of involvement of the different cytologic structures proceeds on an uneven front. The result is different combinations of deficits in hair cells, the stria vascularis, and neurons that for the individual are genotypic and inherited. The functional expressions of the cochlear disorders present a wide spectrum of abnormal pure tone threshold patterns and diminished word discrimination scores.

In previous reports emanating from this laboratory, it was emphasized that presbycusis could be viewed as occurring in four pathologic types or in combinations thereof.[1-5] Three types are based on visual correlations of audiograms and cytocochleograms; thus, abrupt high-tone threshold losses are attributed to sensory cell loss, flat threshold losses to strial atrophy, and diminished word discrimination to loss of cochlear neurons. Because no pathologic correlate is evident for the gradual descending audiometric pattern, it is reasoned that a fourth type of presbycusis is caused by an inner ear conductive disorder that has no pathologic correlate on light microscopy.

We have examined a larger number of cases of presbycusis that reside in the temporal bone collection at the Massachusetts Eye and Ear Infirmary and have correlated the audiometric test data with quantitative assessments of cochlear disorders. The results of these studies show that the concept of four predominant pathologic types is valid; however, it is clear that many cases show mixtures of these types, and furthermore, in about 25% of cases the cochlear changes on light microscopic examination are not adequate to explain the hearing losses.

MATERIALS AND METHODS

A survey of the entire collection of 1,500 serially sectioned temporal bones reveals 21 cases that meet the criteria of having sensorineural hearing losses characterized by insidious onset, bilateral symmetry, and progression into old age without any clinical evidence of other ear disorders. The age, sex, occupation, test to autopsy interval, and cause of death for each case is presented in Table 1. The number of cases is too small for statistical analysis; therefore, visual correlations of the audiometric data and cytocochleograms form the basis for our judgments. The pairs of cochleae show similar pathologic changes; therefore, the cochlea of each pair judged to have the best histologic preservation and preparation has been chosen for quantitative cytologic study.

The 8-kHz frequency was uniformly poorly heard in all of these aged individuals. The thresholds for this frequency ranged from 60 dB to 100 dB for an average of 75.8 in 17 cases. In 4 cases, the tone was not heard at maximum stimulation intensities. For this reason 8 kHz does not play a significant role in our differentiation of different pathologic types of presbycusis. A casual inspection of the audiograms and related cytocochleograms shows that a loss of

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TABLE 1. PATIENT DATA

Type of Presbycusis	Case	Age	Sex	Occupation	TAI	Cause of Death
Sensory	1	93	M	Shoemaker	10 y	Cardiac failure
Neural	2	71	M	Shipyard carpenter	16 y	Gastric cancer
	3	81	M	Factory worker	13 y	Cardiac failure
	4	91	F	Unknown	7 mo	Bronchopneumonia
Strial	5	76	F	Homemaker	3 y	Hepatic cancer
	6	72	F	File clerk	4 y	Myocardial infarct
	7	72	M	Military service	3 y	Cerebral hemorrhage
	8	73	F	Homemaker	5 y	Gastric hemorrhage
Cochlear conductive (hypothetical)	9	91	M	Unknown	6 mo	Pulmonary embolus
	10	90	F	Store manager	8 mo	Myocardial infarct
	11	87	M	Prize fighter, cook	1 yr	Pulmonary cancer
Mixed	12	89	F	Seamstress	2 mo	Cardiac failure
	13	81	F	Musician	18 mo	Myocardial infarct
	14	82	M	Construction riveter	11 y	Leukemia
	15	85	F	Unknown	11 mo	Cardiac failure
	16	96	F	Factory seamstress	4 y	Cardiac failure
Indeterminate	17	89	M	Factory worker	16 y	Pulmonary cancer
	18	85	F	Stockbroker	5 y	Cardiac failure
	19	75	F	Homemaker	1 mo	Pharyngeal cancer
	20	84	M	Attorney	2 y	Myocardial infarct
	21	67	F	Homemaker	6 mo	Colonic cancer

TAI — test to autopsy interval.

cochlear neurons shows little or no quantitative relationship to elevation of thresholds for pure tones, but is expressed audiometrically in terms of diminished word discrimination scores.

All of the temporal bones had been prepared by the standard method of being decalcified, embedded in celloidin, and serially sectioned in the horizontal plane at a thickness of 20 μm. Every 10th section was stained with hematoxylin and eosin and mounted on a glass slide. The cochleae were graphically reconstructed according to the method of Guild[6] and Schuknecht.[7,8] Inner and outer hair cells were plotted separately as being present or absent. The neuronal populations were counted with the aid of an ocular grid and multiplied by 10. A correction factor of 0.9 was used to compensate for neurons located at the interface of sections, where they would be subject to double counting. The method of Otte et al[9,10] was used to display the neuronal data. In this method a vertical line is drawn through the neuronal spiral reconstruction to divide the spiral ganglion into four segments, and the total count for each segment is determined. For a 32-mm-long cochlea, these segments provide innervation for the organ of Corti approximately as follows: segment 1, 0 to 6 mm; segment 2, 6 to 15 mm; segment 3, 15 to 22 mm; and segment 4, 22 to 32 mm. Segmentalizing the neuronal counts minimizes the inaccuracies of attempting to spatially correlate the spiral ganglion with the organ of Corti on a more precise basis. The stria vascularis was plotted in terms of estimated loss of volume of strial tissue, with no attempt to differentiate the three cell types (marginal, intermediate, basal) that constitute this organ.

The data on the hair cells, neurons, and the stria vascularis were transferred to histograms in which black filling indicated the percent loss as a function of distance along the cochlear duct as measured from the basal end. The total loss of strial tissue for each cochlea was determined by measuring the percent of black filling in the histogram with an image analysis computer system (Zeiss Videoplan I, CPU-Z80). The neuronal populations were plotted as losses compared to the mean for neonatal cochleae. The length of the cytocochleogram was expanded or contracted overall, if necessary, to fit our 32-mm graphic format. The 21 cochleae undergoing study varied in length from 26.7 to 36 mm, for an average of 32.2 mm. The audiogram for each case was placed on a parallel coordinate of equal length to the cytocochleogram, with frequency located on a data-based anatomic frequency scale. The final product for each cochlea is a cochlear chart consisting of matching audiogram and cytocochleogram.

RESULTS

We established a set of criteria for significant pathologic change based on factors that we believe are reasonable but admittedly somewhat arbitrary. The criterion for sensory presbycusis is the presence

TABLE 2. FINDINGS USED FOR CLASSIFICATION

Type of Presbycusis	*Case*	*Age*	*Sex*	*Sensory Lesion (mm)*	*Strial Loss (%)*	*Neuronal Count*	*Neuronal Evaluations as % Less or (More) Than Normal Means for*	
							Birth	*Same Age*
Sensory	1	93	M	11.5*	28.9	18,315	48	(10)
Neural	2	71	M	2.5	0	3,924	89*	81
	3	81	M	3	0.5	12,645	64*	32
	4	91	F	4	9.2	6,111	83*	63
Strial	5	76	F	4	77.1*	18,126	49	13
	6	72	F	4	51.2*	26,667	25	(28)
	7	72	M	1.2	44*	24,903	30	(19)
	8	73	F	0	35.4*	21,891	38	(5)
Cochlear conductive (hypothetical)	9	91	M	1	24.9	23,526	34	(42)
	10	90	F	3	23.2	20,493	42	(10)
	11	87	M	6.5	6.3	21,071	41	(13)
Mixed	12	89	F	3.5	40.3*	15,745	56*	16
	13	81	F	1	42.9*	9,765	73*	48
	14	82	M	12*	7.9	12,429	65*	34
	15	85	F	12*	33.1*	15,552	56*	17
	16	96	F	12*	31.2*	16,173	55*	3
Indeterminate	17	89	M	4	20.7	18,225	49	3
	18	85	F	5	12.4	19,044	46	(2)
	19	75	F	4	15.6	25,704	28	(24)
	20	84	M	2.5	18	23,121	35	(24)
	21	67	F	2.1	17.9	17,937	49	(12)

*Meeting our arbitrary criteria for significant pathologic change.

of any total loss of hair cells beginning at the basal end of the cochlea that is at least 10 mm in length so as to encroach on the speech frequency area of the cochlea. For neuronal presbycusis the criterion is a loss of 50% or more of cochlear neurons compared to the mean for neonates (35,500). This figure receives some support from the studies of Otte[9] and Pauler et al,[11] in which word discrimination appeared to be diminished with neuronal counts in the range of 15,000 to 20,000. The criterion for strial presbycusis is a loss of 30% or more from the normal volume of strial tissue. This figure is based on the findings of Pauler et al,[12] who showed that hearing losses occurred when there were strial losses of about 30% or greater.

Cochlear conductive presbycusis required both functional and pathologic criteria. The functional criterion is an arbitrary requirement that the audiogram show a linear gradually descending slope over at least a five-octave range, with a difference of at least 50 dB between the best and poorest thresholds and no more than a 25-dB difference between any two adjacent octaves. The pathologic criterion is a requirement that the cochleae must not meet any of the criteria set for significant pathologic change in the sensory cells, neurons, or stria vascularis as described above.

When the cases met the criteria for significant pathologic change in more than one structure, they were classified as mixed presbycusis. Those cases in which cochlear changes did not reach significant levels in any structure, and in which the audiometric thresholds did not meet the criteria for the gradual descending audiogram of cochlear conductive presbycusis, were classified as indeterminate presbycusis.

The quantification of the pathologic changes provides numeric values that are used to classify the 21 cases into one of the six types of presbycusis. The data are presented in Table 2.

Sensory Presbycusis. Sensory cell losses at the extreme basal end of the cochlea are a common occurrence in the aging cochlea; however, the area of involvement rarely extends far enough from the basal end to reach the speech frequency area of the cochlea. Many cochleae of aging persons demonstrate an island of hair cell loss in the 8- to 12-mm region, which tonotopically serves the 4-kHz frequency. We attribute this lesion to acoustic trauma. In cases of severe acoustic trauma the lesion can spread basalward to merge with the sensory presbycusic lesion. In such cases it is not possible to determine to what extent presbycusis and acoustic trauma have played independent causal roles, because the pathologic features

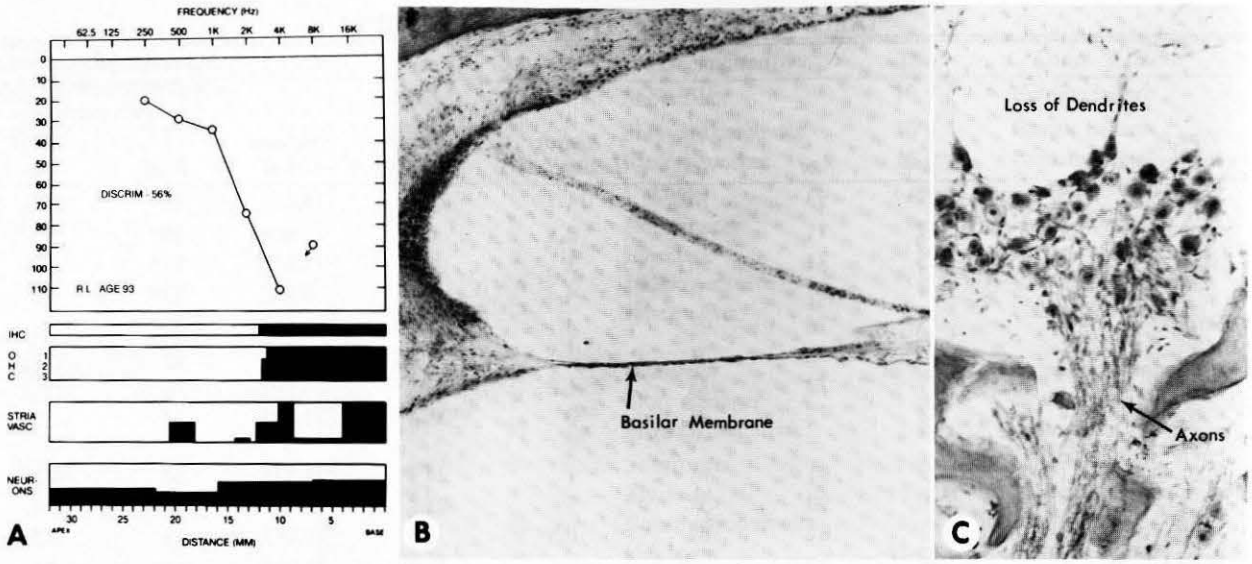


Fig 1. (Case 1) Sensory presbycusis in 93-year-old man. A) Sensory lesion is 12 mm in length. Losses of neurons (48%) and stria (28.9%) do not meet our levels of pathologic significance. B) This view in 8-mm region shows total atrophy of organ of Corti (x57). C) There is retrograde neuronal degeneration in basal turn; note loss of dendritic fibers (x240).

of each are similar. In this case the otologic history may be a more reliable determinant of causation.

The earliest changes, such as a loss of stereocilia, are detectable only by electron microscopy.[13] This is followed by slight distortion and flattening of the organ of Corti and then by a loss of supporting and sensory cells. Eventually the organ of Corti appears as an undifferentiated epithelial mound on the basilar membrane, and it may disappear completely from the basal end of the cochlea. There is a concomitant loss of cochlear dendrites and, to a lesser extent, of neuronal cell bodies that parallels closely the spatial distribution and magnitude of atrophy of the supporting cells of the organ of Corti. Wright et al[14] found a generalized and gradual reduction in the outer hair cell density with age, but with an additional loss in the elderly at the base and to a lesser extent at the apex. The apical loss is apparently restricted to persons over 70 years of age. In our cases, the apical hair cell loss is minimal and insignificant. For the inner hair cell loss, the decline is less marked but follows the same pattern.

Microscopists observed long ago that lipofuscin accumulates in the tissues of aged individuals; hence its popular synonym "wear and tear pigment" and its German name *Abnutzungspigment*.[15-17] Ishii et al[18,19] have shown that lipofuscin granules accumulate in the apical cytoplasm of the hair cells and supporting cells of the organ of Corti and the vestibular sense organs of the aging ear. It was not demonstrable in individuals under the age of 6 years, but increased in quantity as a function of age. The location of the lipofuscin granules correlated with the location of lysosomes and was therefore assumed to be a waste product of lysosomal activity. Lysosomes are rich in acid hydrolases, and at least 16 different enzymes have been identified in them.[20] Bennett[21] was the first to suggest that insoluble end products of metabolism accumulate in lysosomes. It would seem reasonable that these changes are a reflection of exhaustion of enzymatic activity and an important cause of cell death.

Case 1 meets our criteria for sensory presbycusis, that is, an uninterrupted loss of hair cells at the basal end involving at least a 10-mm area (Fig 1). Sensory presbycusis also appears as a component of mixed presbycusis in cases 14, 15, and 16 (Table 2).

Neural Presbycusis. Otte et al[10] counted the neurons in cochleae from 100 hearing ears from subjects whose ages spanned nine decades and in whom there was no evidence of disease affecting the neurons. The populations ranged from 36,918 for those in the first decade to 18,626 for those in the ninth decade, for a linear progressive loss of about 2,100 neurons per decade (Fig 2).

A loss in population of cochlear neurons in the presence of a functional end organ creates a distinctive pattern of auditory dysfunction characterized by a progressive loss of word discrimination in the presence of stable pure tone thresholds. Gaeth[22] has used the term phonemic regression to describe this phenomenon. Palva and Jokinen[23] found the word discrimination scores of patients over 60 years of age to be better in the left ear and attributed this to left cerebral dominance becoming manifest as the result of degenerative change in the auditory pathways. Elderly patients with rapidly progressive neural presbycusis often demonstrate associated diffuse degenerative changes of the central nervous system, exhibited by motor weakness and lack of coordination,

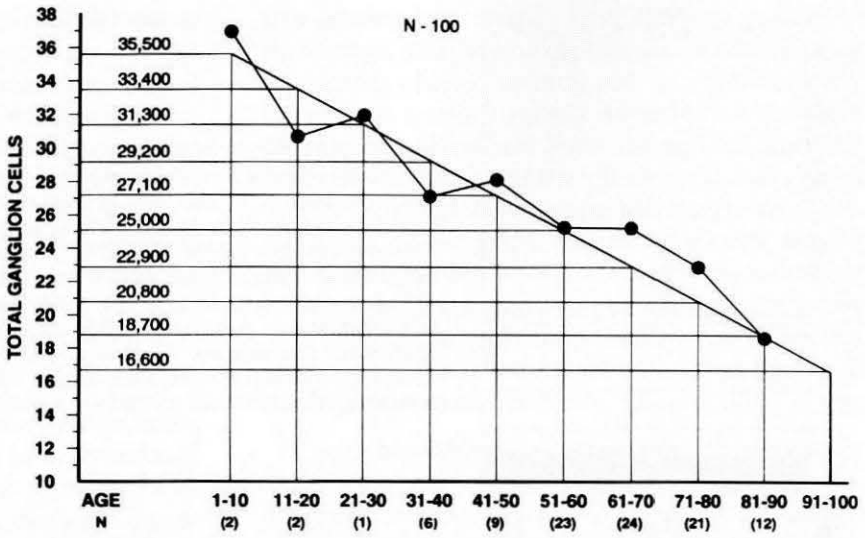


Fig 2. Cochlear neuronal populations as function of age. Means show uniform loss of about 2,100 neurons per decade. Mean for 10th decade is extrapolated.

tremors, irritability, loss of memory, and intellectual deterioration. Neural presbycusis is characterized by a progressive loss of neurons throughout the cochlea with only a very slight tendency to be more severe at the basal end.[24]

The loss of cochlear neurons is the most consistent pathologic change in the aging ear. It begins at an early age and continues throughout life. The pure tone thresholds are variable, and it seems quite clear they are not affected by neuronal loss until about 90% have disappeared.

The fact that the neurons that remain retain their dendritic fibers indicates that the missing neurons had undergone total degeneration (soma, axon, and dendrite).

Pauler et al[11] correlated neuronal populations with speech discrimination scores in 28 elderly persons. The neuronal counts were summed for four regions of the cochleae (0 to 6 mm, 6 to 15 mm, 15 to 22 mm, and 23 mm to the apex). A loss of cochlear neurons in the 15- to 22-mm region (the locus for the speech frequencies) correlated positively with a loss of word discrimination, whereas losses in the other regions did not.

Saccular degeneration involving both sensory and neural structures can occur concomitantly with cochlear degeneration as an aging process in both human subjects and animals.[25,26]

The neuronal losses in the auditory system that occur with aging are not limited to the periphery. Arnesen[27] calculated the total numbers of neurons in the ventral and dorsal cochlear nuclei from serial sections in six subjects 76 to 89 years of age. There was about a 50% loss of neurons compared to the numbers calculated for normal subjects by other investigators.

Cases 2, 3, and 4 meet our criteria for neural presbycusis, that is, a loss of 50% or more of cochlear neurons when compared to the mean for normal neonatal ears (Fig 3). Neural presbycusis also occurs as a component of mixed presbycusis in cases 12 to 16 (Table 2).

Strial Presbycusis. Atrophy of the stria vascularis is a common pathologic entity often affecting several members of a family. Typically, the hearing loss has an insidious onset in the third to sixth decades of life and progresses slowly. The clinical feature that distinguishes it from other types of presbycusis is the flat or slightly descending pure tone threshold audiometric pattern associated with excellent word discrimination scores. The findings indicate that ears with strial atrophy, when stimulated within their sensitivity ranges, are capable of accurate stimulus coding. Although the small increment sensitivity index test is usually positive for loudness recruitment, these patients do not complain of discomfort from loud sounds or of distortion. They respond well to the use of amplification and may be given a good prognosis for retaining useful hearing into old age.[2,5,28] Pauler et al[12] performed a quantitative study of strial tissue in 24 cochleae and found that the magnitude of strial atrophy correlated positively with the extent of elevation of pure tone thresholds.

Typically, there is patchy atrophy of the stria vascularis in the middle and apical turns of the cochlea.[8] There may be partial or complete loss of strial cells, sometimes with cystic structures and occasionally with basophilic deposits.

Takahashi[29] used the electron microscope to study the stria vascularis in temporal bones of persons over the age of 60. He demonstrated two types of atrophy: 1) a patchy type most severe in the apical and extreme basal regions and 2) a diffuse type often showing

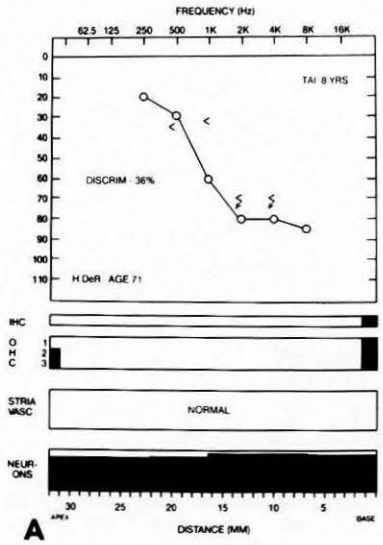
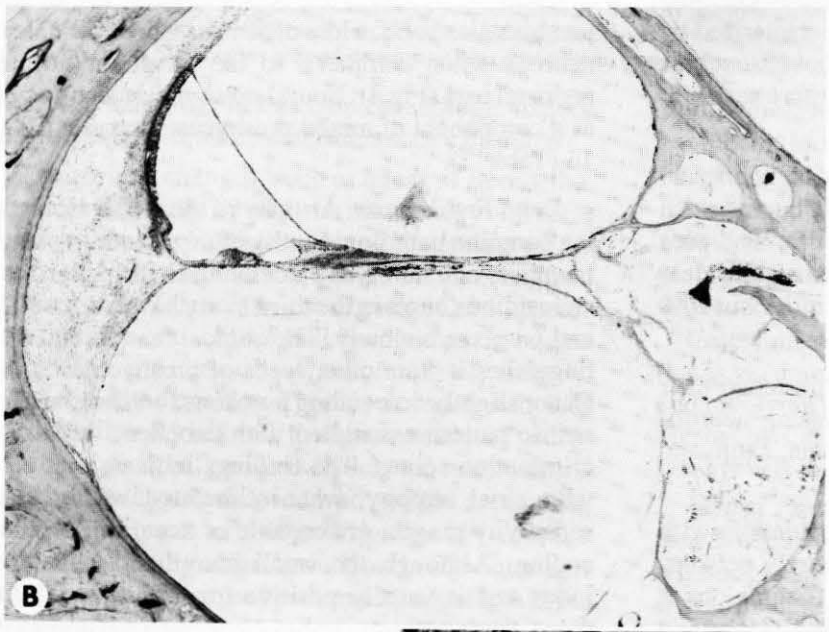
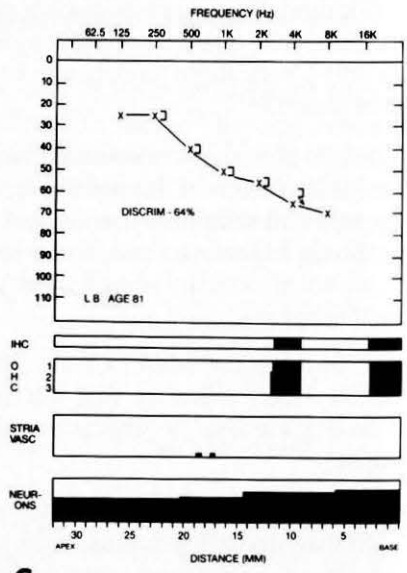
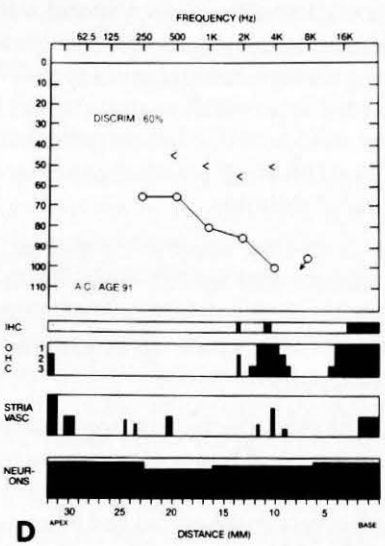
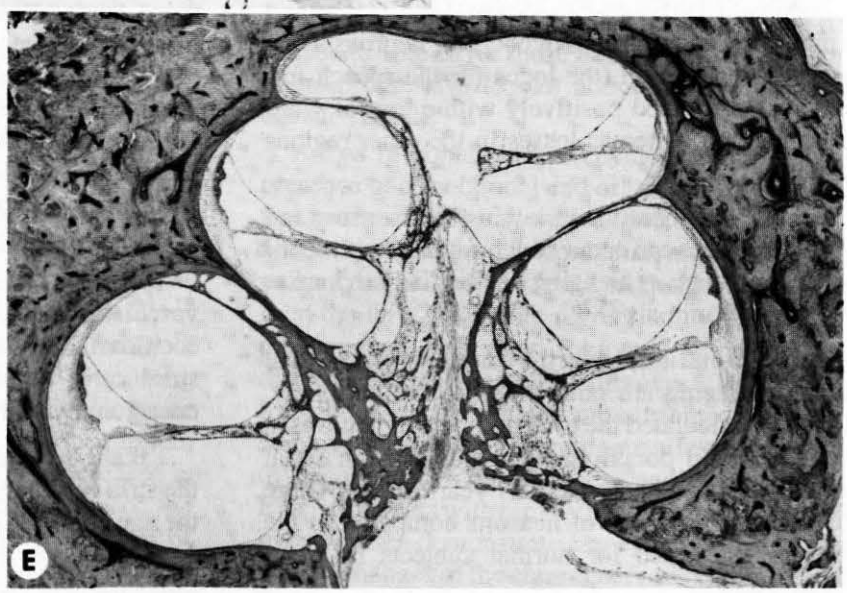


Fig 3. Neural presbycusis. A,B) (Case 2) 71-year-old man. A) Total neuronal loss is 89% of mean for neonatal normal. Sensory cell loss is minimal and stria is normal. TAI — test to autopsy interval. B) This view of 12-mm area shows normal organ of Corti and stria vascularis and near-total loss of cochlear neurons (x48). C) (Case 3) 81-year-old man. Total neuronal loss is 64% of mean for neonatal normal. Sensory and strial lesions are insignificant. There is 3-mm acoustic trauma lesion in 9- to 12-mm region. D,E) (Case 4) 91-year-old woman. D) Total neuronal loss is 83% of mean for neonatal normal. Four-millimeter sensory presbycusis and 3-mm acoustic trauma lesions are considered to be functionally insignificant. Apparent conductive hearing loss is believed to be artifact caused by pressure occlusion of ear canal by ear phone. E) This midmodiolar view shows normal organ of Corti and severe loss of cochlear neurons (x19).









normal strial thickness with large intercellular spaces that might not be visible by light microscopy. Kimura and Schuknecht,[30,31] using electron microscopy, found similar atrophic changes in surgical specimens of the cochleae of persons who had Meniere's disease and underwent labyrinthectomy and assumed they represented alterations of aging rather than Meniere's disease. All three cell layers of the stria were involved in various degrees and combinations; however, the marginal cells appeared to be most severely affected. In some regions of atrophy the stria consisted of only a layer of basal cells lining the endolymphatic space.

Probably the loss of strial tissue affects some quality of endolymph that results in a detrimental influence on the physical and chemical processes by which energy is made available to the sense organ. Experimental observations permit several interesting speculations on the functional significance of the stria vascularis. First, the stria vascularis appears to be the source of the positive 80-mV DC potential of the scala media.[32-34] Second, the stria vascularis has long been thought to be the site of endolymph formation.[35] Von Fieandt and Saxén,[36] using light microscopy, and later Engström et al[37] and Smith,[38] using electron microscopy, showed that the stria vascularis has morphologic features consistent with secreting organs in other parts of the body. Smith[38] has shown that the marginal cells that face the endolymph surround the capillary networks, with their basal surfaces exhibiting numerous extensions and infoldings in the basal plasma membrane that interdigitate with other cells, including the capillary endothelial cells. The implication of a secreting function is found in the fact that this type of structure is present in kidney tubules,[39] serous alveoli, choroid plexus, ciliary bodies, and secretory ducts of the submaxillary gland. Third, the tissues of the stria vascularis contain large amounts of oxidative enzymes that are required for glucose metabolism and that may be essential for the production of energy to support cochlear function.[40] These observations assign an important functional role to the stria vascularis.

Cases 5 to 8 meet our criteria for strial presbycusis, that is, a 30% or greater loss of strial tissue (Fig 4). Strial presbycusis also appears as a component in mixed presbycusis in cases 12, 13, 15, and 16 (Table 2).

Cochlear Conductive (Hypothetical) Presbycusis. Cochlear conductive presbycusis is differentiated from the indeterminate group by having linear descending audiograms. The diagnosis is derived by histologic exclusion of any consistent light microscopic explanation for the gradual descending pure tone threshold type of hearing loss. Cochlear conductive hearing loss usually first becomes evident in middle age, and the hearing loss shows almost equal increments of loss for each octave, with word discrimination scores inversely related to the steepness of the threshold gradient. Ramadan and Schuknecht[41] compared the temporal bone findings in two groups of elderly individuals with symmetric high-tone hearing losses. In the group that had gradually sloping threshold losses they were unable to detect a pathologic correlate by light microscopy, whereas the group with abrupt threshold losses had hair cell losses that were tonotopically consistent with those known to result from acoustic trauma.

Cases showing gradual descending threshold patterns, often characterized by straight descending audiograms, consistently fail to show any pathologic correlate. This type of hearing loss not only occurs as a manifestation of aging but is common in association with otosclerosis and Paget's disease of the temporal bone. Because the increments of loss show a linear relationship to frequency, it is speculated that the loss is caused by alterations in the resonance characteristics of the cochlear duct that determine frequency distribution. An attractive candidate for such an alteration is the basilar membrane, which features a nearly linear increase in width[42] and decrease in elasticity[43] from base to apex. It seems reasonable to attribute the linearity of the descending audiogram to degradation in compliance of the cochlear duct rather than to a spatially linear cellular loss or dysfunction. For these reasons, the term cochlear conductive presbycusis seems appropriate for these cases.

The question arises as to whether these hearing losses could be attributed to lesions of the cortical or subcortical auditory systems. It has been demonstrated in animal experiments that bilateral ablation of the auditory cortex does not alter pure tone thresholds. Large lesions at or below the level of the tectum produce pure tone threshold losses; however, transection of the brachium of the inferior colliculus and transection of the auditory commissures of the medulla have little or no effect on pure tone thresholds. In humans, evidence linking central lesions to a specific type of audiometric pattern is lacking. A concept has evolved among researchers that cortical and subcortical lesions of the auditory pathways affect the ability to discriminate complex acoustic patterns (eg, sound localization, discriminations involving pitch, loudness levels) but have little or no effect on pure tone thresholds.[44]

Mayer[45] suggested that impaired hearing of old age might be due to stiffening of the basilar membrane and supported his thesis with histologic sections that he interpreted as showing calcification of

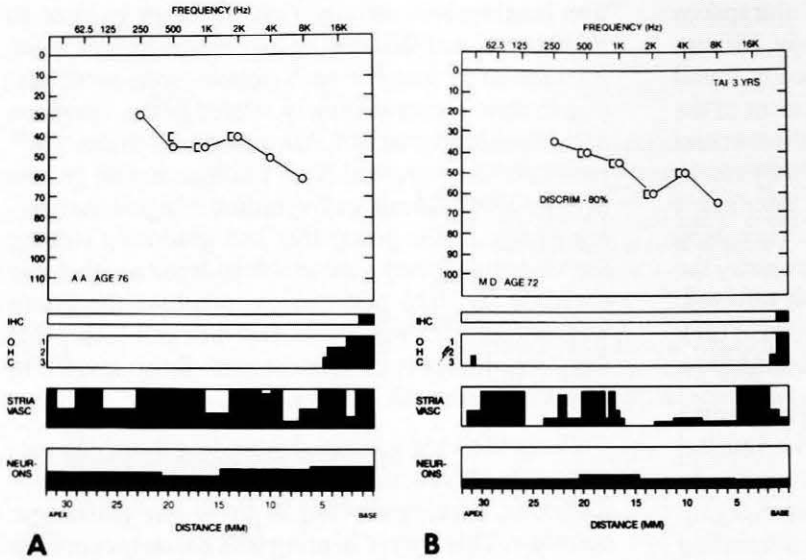
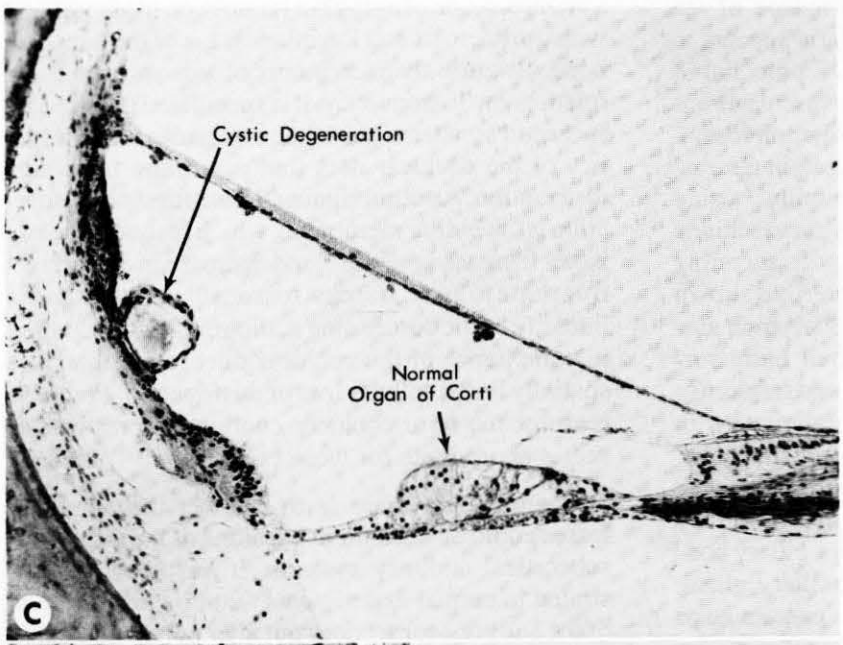
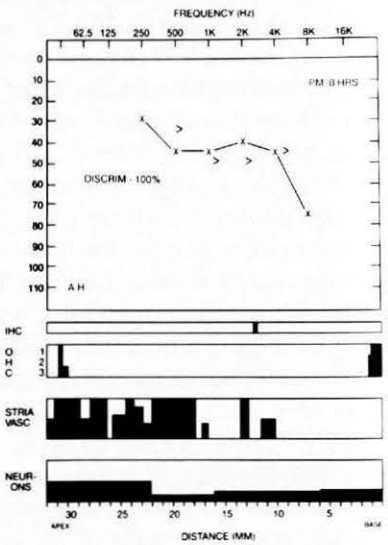
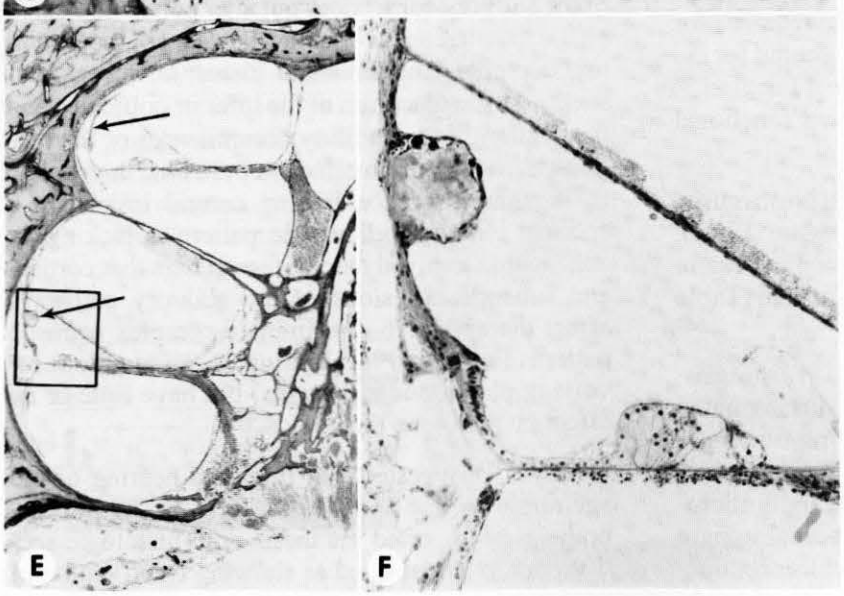
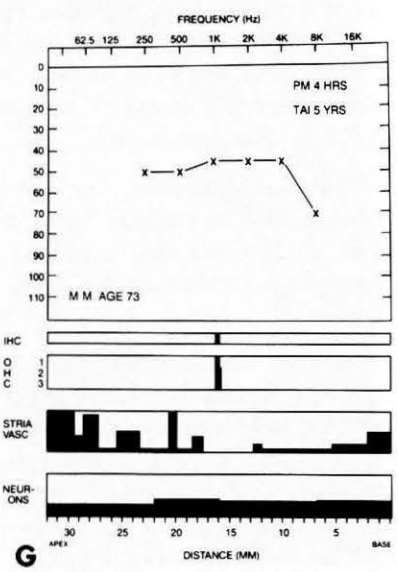


Fig 4. Strial presbycusis. A) (Case 5) 76-year old woman. Loss of stria is estimated to be 77.1%. Losses of sensory cells (4 mm) and neurons (49%) are not significant by our criteria. B,C) (Case 6) 72-year-old woman. B) Loss of stria is estimated to be 51.2%. Losses of sensory cells (1.2 mm) and neurons (25%) are not significant by our criteria. C) This view of middle turn shows partial cystic degeneration of stria vascularis. Organ of Corti is normal (x119). D-F) (Case 7) 72-year-old man. D) Loss of stria is estimated to be 44%. Losses of sensory cells (1.2 mm) and neurons (30%) are not significant by our criteria. PM — postmortem. E,F) This view shows severe loss of strial tissue (arrows in E) in otherwise normal cochlear duct. E) Magnification x14. F) Boxed area of E (x112). G) (Case 8) 73-year-old woman. Strial loss is judged to be 35.4%. Sensory and neuronal losses are insignificant by our criteria.









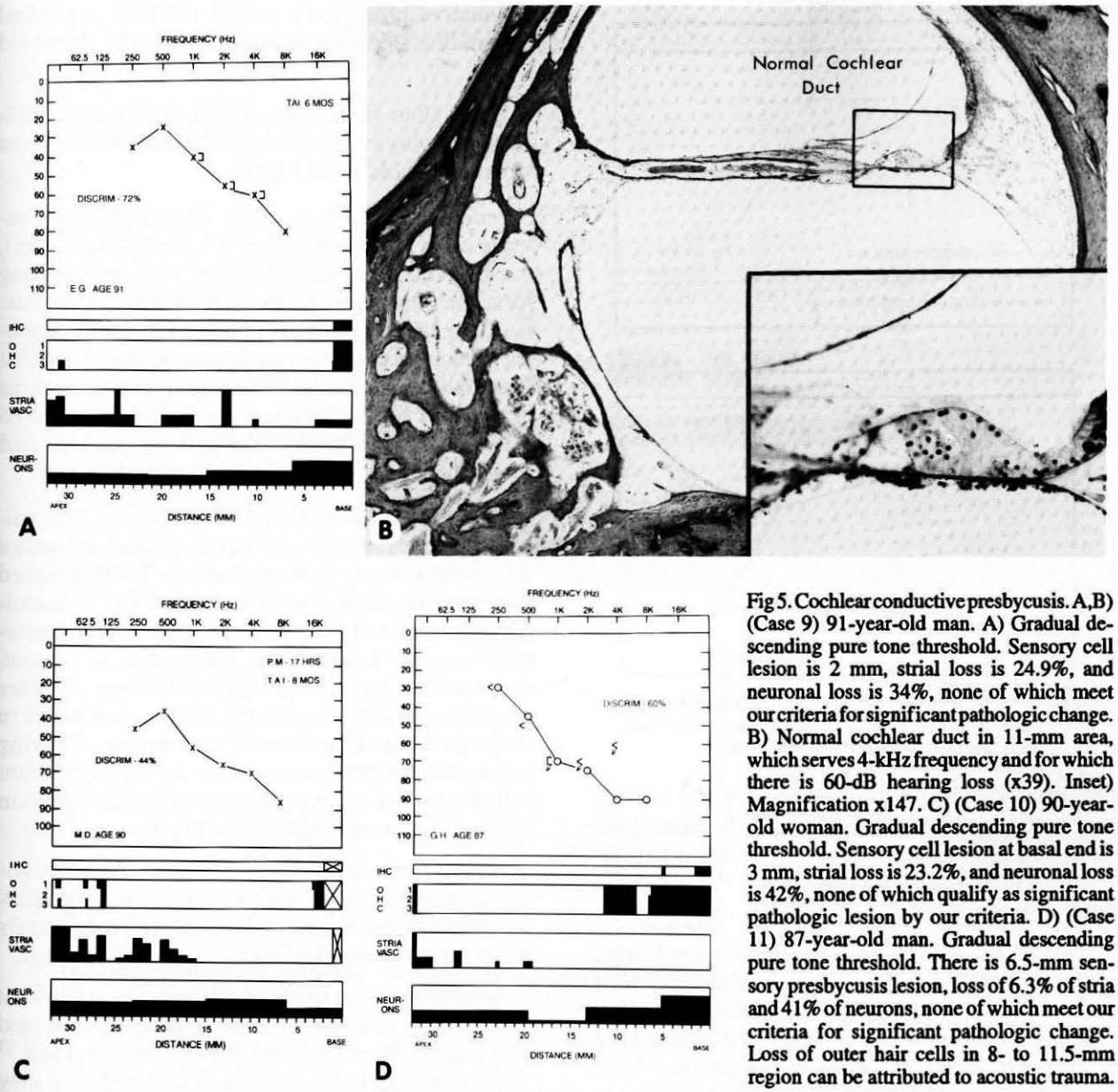


Fig 5. Cochlear conductive presbycusis. A,B) (Case 9) 91-year-old man. A) Gradual descending pure tone threshold. Sensory cell lesion is 2 mm, strial loss is 24.9%, and neuronal loss is 34%, none of which meet our criteria for significant pathologic change. B) Normal cochlear duct in 11-mm area, which serves 4-kHz frequency and for which there is 60-dB hearing loss (x39). Inset) Magnification x147. C) (Case 10) 90-year-old woman. Gradual descending pure tone threshold. Sensory cell lesion at basal end is 3 mm, strial loss is 23.2%, and neuronal loss is 42%, none of which qualify as significant pathologic lesion by our criteria. D) (Case 11) 87-year-old man. Gradual descending pure tone threshold. There is 6.5-mm sensory presbycusis lesion, loss of 6.3% of stria and 41% of neurons, none of which meet our criteria for significant pathologic change. Loss of outer hair cells in 8- to 11.5-mm region can be attributed to acoustic trauma.

the basilar membrane. Crowe et al found partial atrophy of the cochlear nerve to the basal turn to be a prominent lesion in the majority of ears with descending audiometric thresholds, but noted that "some ears with the gradual type of loss do not have sufficient degree of nerve atrophy to explain the impairment of hearing."[46(p374)] They also reported finding hyalinization and deposition of calcium salts in the basilar membrane at the basal end of the cochlea to be more common in patients with descending audiometric patterns than in normal ears or ears with abrupt high-tone hearing losses. Covell and Rogers[47] and Pestalozza et al,[48] in studies on senile guinea pigs, found that the losses in cochlear microphonic response were greater than could be attributed to hair cell changes and suggested that conductive lesions might be present. Glorig and Davis[49] accept the idea of an inner ear conductive impairment as being logical. In support of this concept they observed that loudness recruitment is absent in many cases of presbycusis.

Nomura[50] found neutral fat and cholesterol in the filamentous structure of the pars pectinata of the basilar membrane in 9 of 20 aged patients. He considered this lipidosis of the basilar membrane to represent an alteration of aging that might cause hearing loss. Kraus[51] has shown that the basilar membrane of guinea pigs exhibits a decrease in density as a function of aging; this finding supports the concept of a physical-chemical alteration in its structural characteristics. Support for the concept of an inner ear conductive hearing loss is found in the light and electron microscopic study of a single cochlea by Nadol.[52] His report concerned an 81-year-old man

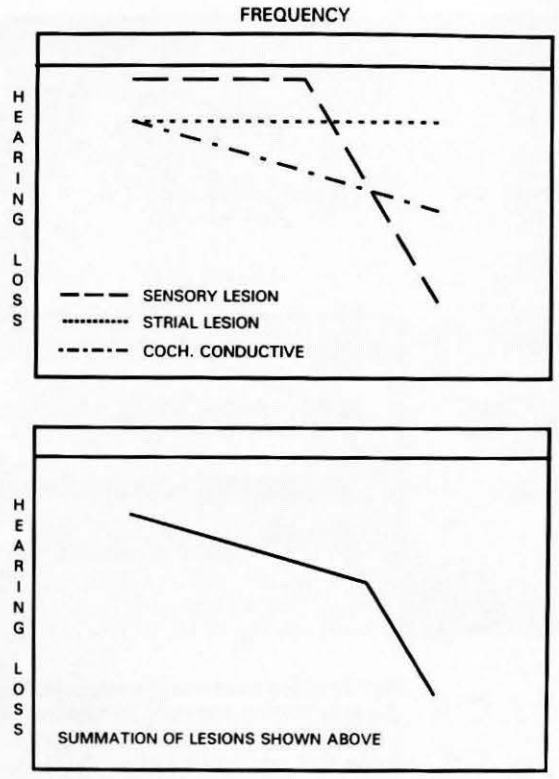


Fig 6. How additive effects of different pathologic types of presbycusis occurring in same cochlea can produce variety of pure tone threshold audiometric profiles.

who by history had a progressive bilateral hearing loss. In addition to severe atrophic changes in the organ of Corti, there was marked thickening of the basilar membrane due to an increase in the number of fibrillar layers.

Cases 9, 10, and 11 meet the criterion of having gradual descending pure tone thresholds as defined in Materials and Methods, and do not meet our criteria for significant pathologic changes (Table 2 and Fig 5). Cochlear conductive presbycusis may also have occurred as a component of pathologic changes in cases 3, 13, and 16.

Mixed Presbycusis. Whereas the four classic types of presbycusis occur in isolation often enough to be recognized as clear clinical and/or pathologic entities, many presbycusic hearing losses present as mixtures of these types. If we accept the existence of a cochlear conductive presbycusis and assume that the different types of presbycusis are additive, the audiometric pattern should reflect the underlying pathologic changes in the cochlea (Fig 6). For example, the combination of sensory and strial presbycusis would cause an abrupt high-tone hearing loss superimposed on a flat threshold loss. A sensory and cochlear conductive presbycusis would present as an abrupt high-tone hearing loss superimposed on a descending threshold audiogram. Strial and cochlear conductive presbycusis would manifest a gradual descending slope superimposed on a flat threshold loss.

Cases 12 to 16 meet the criterion of having significant pathologic changes in more than one cochlear structure (Table 2 and Fig 7).

Indeterminate Presbycusis. Histologic study reveals cases (possibly 25% of all presbycusis cases), mostly with a flat and/or abrupt high-tone hearing loss, that show no consistent pathologic correlate. Audiometrically, they fit into the strial and/or sensory presbycusis categories. It may be speculated that these indeterminate cases represent similar patterns of cochlear dysfunction but are caused by impaired cellular function rather than cellular attrition and therefore are not detectable by light microscopy.

Changes that would elude detection by light microscopy are 1) alterations in intracellular organelles that would impair cell metabolism, 2) diminished numbers of synapses on the hair cells, and 3) chemical alterations in the endolymph. In human postmortem temporal bones, these alterations, if present, could not be identified by light microscopy. Another possibility is alterations in the auditory pathways in the brain. Cases 17 to 21 meet the criterion of having indeterminate presbycusis, that is, no significant pathologic change, as previously defined, to explain the hearing losses (Table 2 and Fig 8).

Other Cochlear Changes With Aging. Almost nothing is known of the effect on hearing of aging alterations in the spiral ligament, Hensen's cells, Reissner's membrane, the tectorial membrane, or the limbus.

Alterations in the spiral ligament are quite constant as an aging process, beginning in childhood and progressing throughout the life of the individual.[53] When these changes occur in a moderate degree they are compatible with normal hearing. The changes appear to be as consistent a function of aging as those that occur, for example, in the skin. The atrophy is most severe in the apical half of the cochlea and is progressively less severe toward the basal end. The earliest alteration is a loss of fibrocytes in the region adjacent to the attachment of the basilar membrane (basilar crest). As the atrophy progresses, a zone of acellularity develops in the midportion of the spiral ligament. There appears to be a loss of fibrocytes, as well as a migration of fibrocytes toward the margins of the ligament. With further change, two distinct zones are seen: a larger, internal zone, remarkable for its acellularity and cystic spaces, and a smaller, external zone containing scattered fibrocytes in a fibrillar stroma. Commonly there is a dense layer of closely packed fibrocytes at the interface between

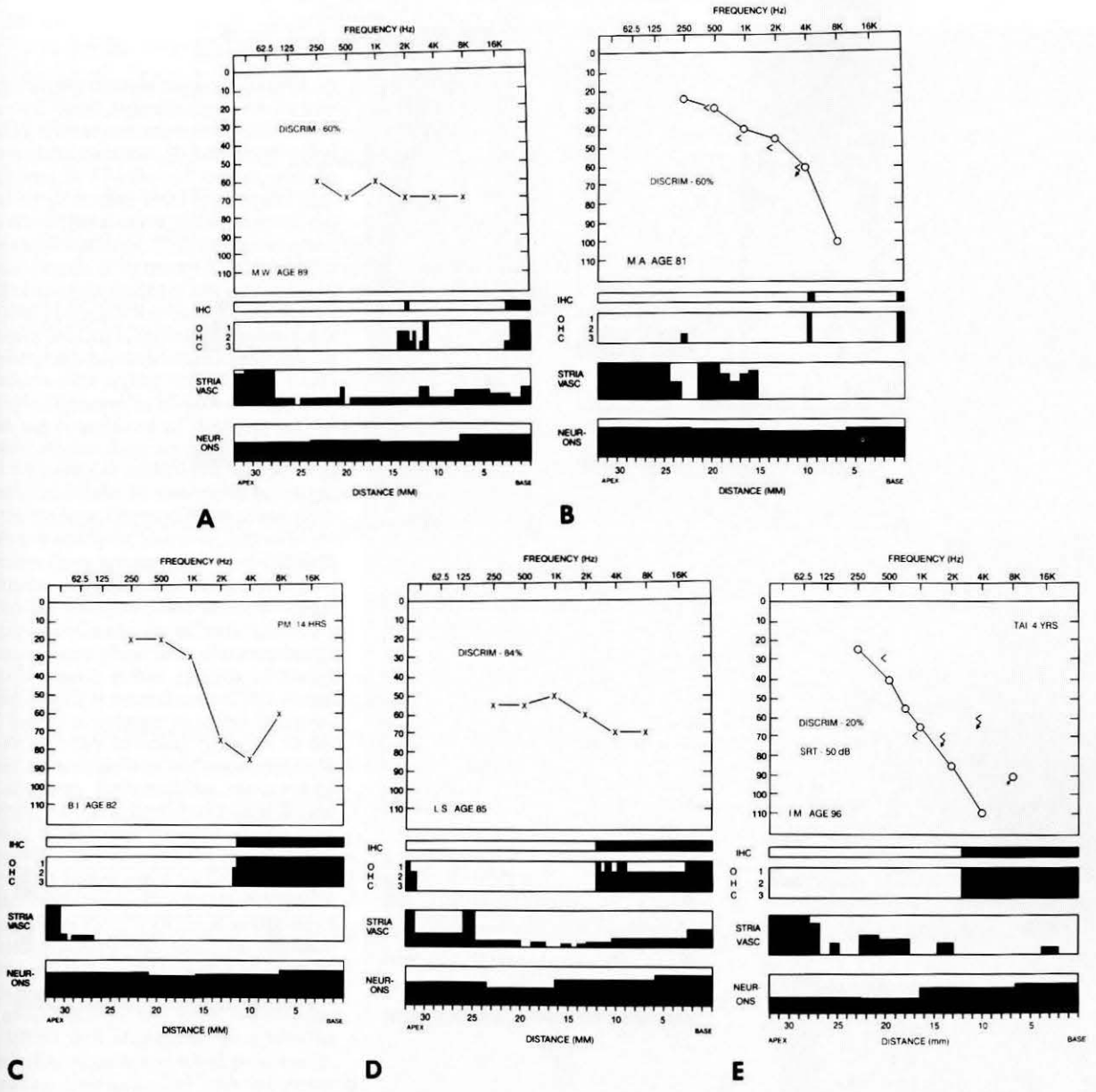


Fig 7. Mixed presbycusis. A) (Case 12) Strial and neural, in 89-year-old woman. There is flat pure tone threshold loss of 60 to 70 dB. There is 40.3% loss of stria and 56% loss of neurons, both of which meet our criteria for pathologic significance. Two-millimeter sensory presbycusis and 3.5-mm acoustic trauma lesions are insignificant. B) (Case 13) Strial and neural, in 81-year-old woman. There is gradual descending threshold pattern that does not satisfy our criteria for cochlear conductive presbycusis in terms of magnitude (see text). Nonetheless, mild cochlear conductive lesion might be present. Strial loss is 42.9% and neuronal loss is 73%, both of which are significant by our criteria. C) (Case 14) Sensory and neural, in 82-year-old man. There is abrupt high-tone hearing loss for frequencies above 1 kHz. Audiogram made 11 years prior to death shows upturn at 8 kHz that suggests that this man, construction riveter, had distinct acoustic trauma lesion at that time, which later merged with sensory presbycusic lesion to produce uninterrupted 12-mm lesion. There is 65% loss of neurons. Both sensory and neural lesions meet our criteria of pathologic significance, whereas strial loss of 7.9% does not. D) (Case 15) Sensory, strial, and neural, in 85-year-old woman. There is flat 50- to 70-dB pure tone threshold. Cochlea shows 12-mm sensory lesion, 33.1% loss of stria, and 56% loss of neurons, all of which are pathologically significant as defined by our criteria. E) (Case 16) Sensory, strial, neural, and cochlear conductive, in 96-year-old woman. This cochlea meets our criteria for all four types of presbycusis. Descending pure tone threshold meets our requirements for cochlear conductive presbycusis, that is, gradient of at least 50 dB over 5-octave range with no more than 25-dB difference between any two adjacent frequencies. There is also 12-mm sensory lesion, loss of 31.2% of stria, and loss of 55% of neurons, all of which are pathologically significant by our criteria.

these zones. All of these changes can be found in normal-hearing ears, but we have the impression that they are more frequent in ears exhibiting descending audiometric patterns. As the spiral ligament shrinks, the configuration of the cochlear duct is altered. Commonly the basilar membrane retains its continu-

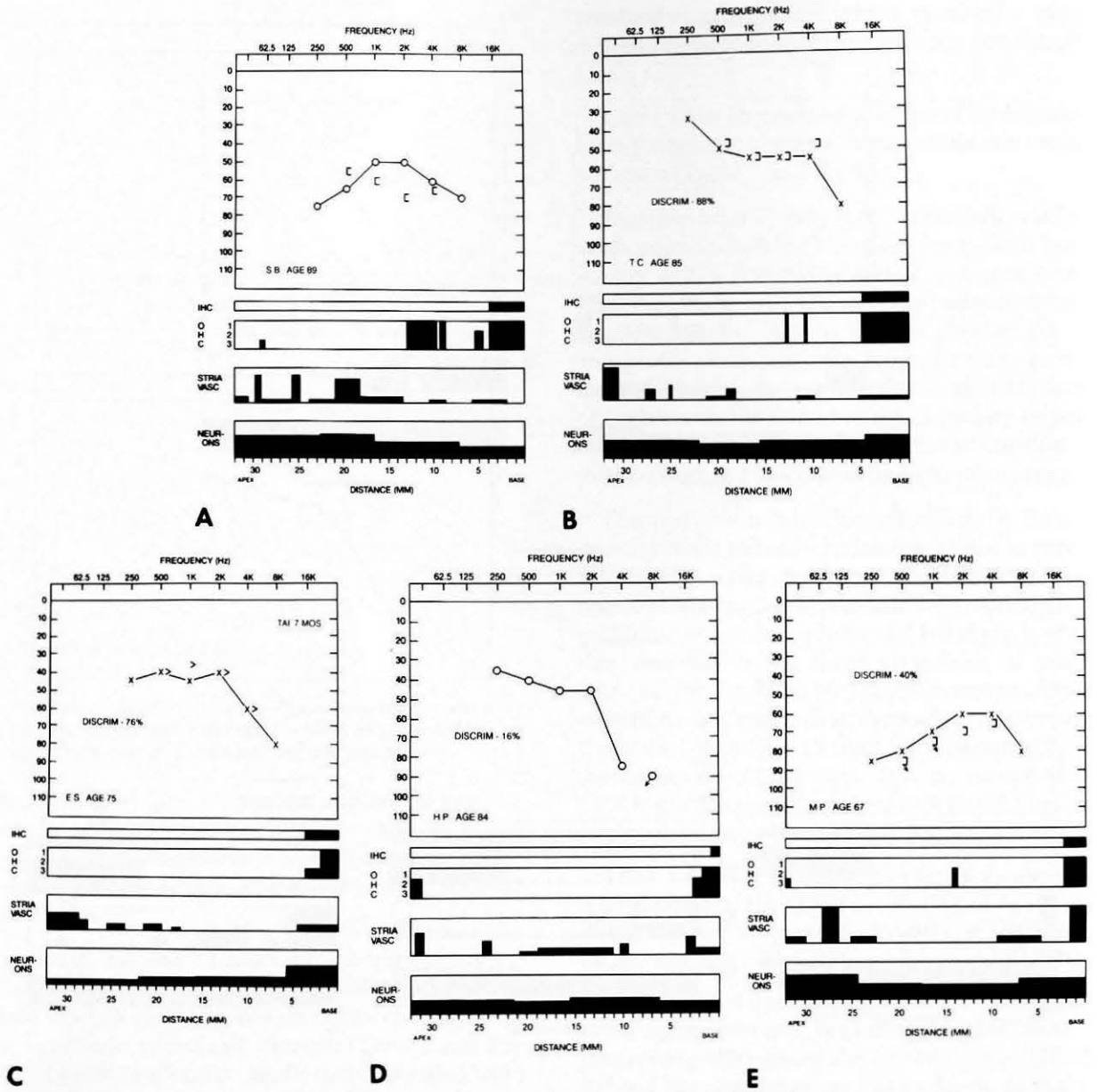


Fig 8. Indeterminate presbycusis. A) (Case 17) 89-year-old man. There is flat pure tone hearing loss. There is 4-mm sensory presbycusic lesion, 20.7% loss of stria, and 49% loss of cochlear neurons, none of which reach our criteria for pathologic significance. There is loss of outer hair cells in 9- to 14-mm region that is consistent with acoustic trauma. B) (Case 18) 85-year-old woman. Mildly descending pure tone threshold is present. There is 5-mm sensory lesion, 12.4% loss of stria, and 46% loss of neurons, none of which reach pathologic significance by our criteria. C) (Case 19) 75-year-old woman. Pure tone thresholds show flat loss up to 2 kHz and descending pattern above 2 kHz. There is 4-mm sensory lesion, 15.6% loss of stria, and 28% loss of neurons, none of which reach pathologic significance by our criteria. D) (Case 20) 84-year-old man. There is mild decreasing pure tone threshold for frequencies up to 2 kHz and abrupt severe loss for higher frequencies. There is 2.5-mm sensory lesion, 18% loss of stria, and 35% loss of neurons, none of which reach pathologic significance by our criteria. E) (Case 21) 67-year-old woman. There is severe hearing loss with slightly ascending pure tone threshold. Cochlea shows 2.1-mm sensory lesion, 17.9% strial loss, and 49% loss of cochlear neurons, none of which reach pathologic significance by our criteria.

ity with the structures of the lateral wall by a thin layer of ligamentous tissue that converts the cochlear duct from a triangular to a flattened shape. Sometimes the basilar membrane separates from the lateral wall by a break in the area between the basilar crest and the spiral prominence. This brings the endolymphatic space into continuity with cystic spaces in the spiral ligament. When this happens, the only remaining connection of the basilar membrane with the bony cochlear wall is a thin layer of spiral ligament tissue bordering the scala tympani. The functional effects of lesions of this type are not known. Rupture of the cochlear duct and profound hearing loss may be the ultimate, but rare, end result of advanced atrophy of

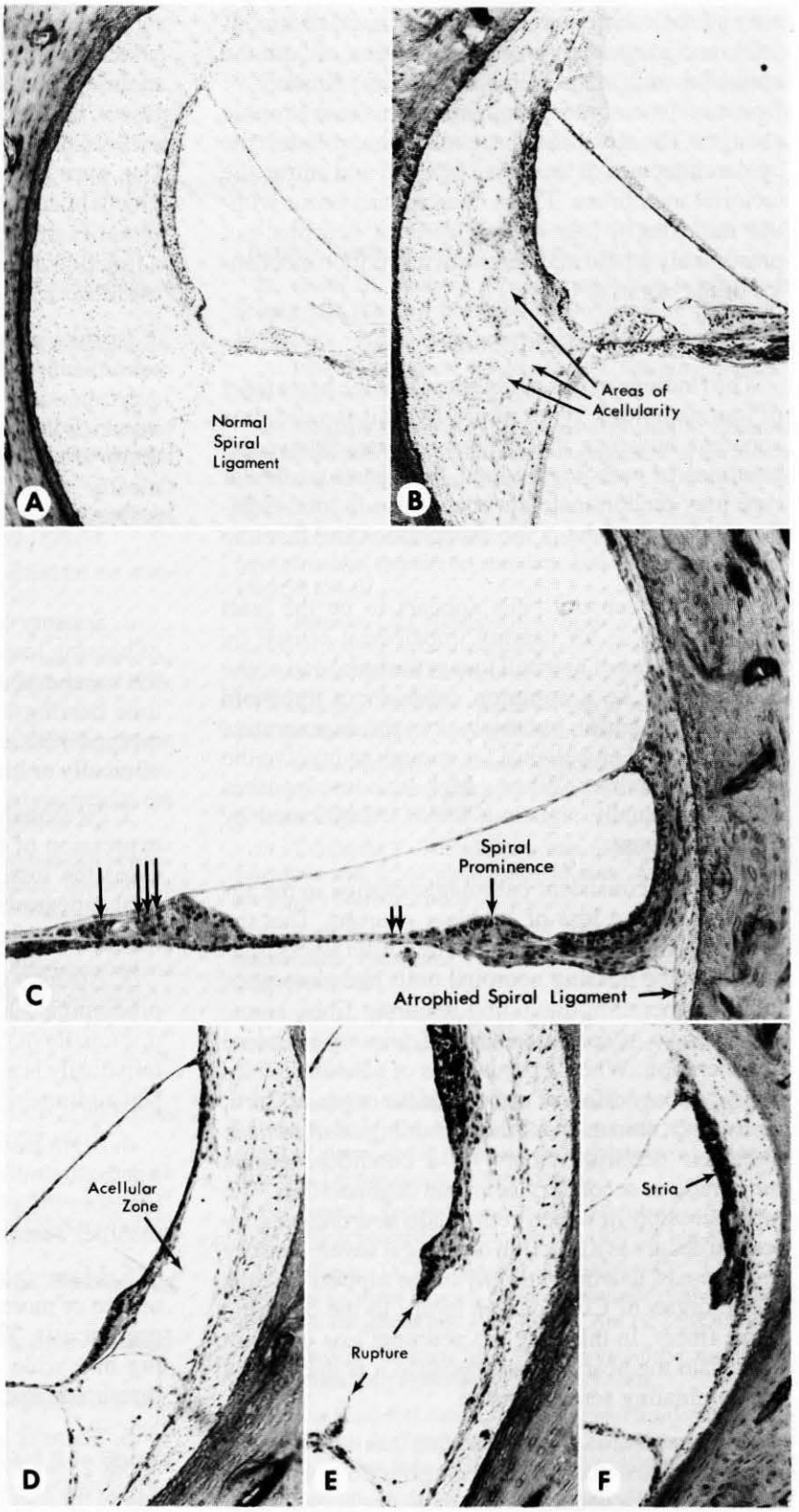


Fig 9. Aging changes in spiral ligament. A) Normal spiral ligament in newborn boy (x71). Fibrocytes are evenly distributed throughout structure. B) Atrophy of spiral ligament in 77-year-old woman with no history of hearing loss (x71). Spiral ligaments of basal turns show areas of decreased cellularity, while adjacent areas show strands of increased cellularity. This is normal aging process and appears to be result of migration and clustering of fibrocytes. Often, densest accumulation of fibrocytes is in substrial area. Structures of cochlear duct appear normal. C) Atrophy of spiral ligament in 36-year-old man who had not complained of deafness (x136). Both cochleae show severe atrophy of spiral ligaments in middle and apical turns. Cochlear duct in 18-mm region of left ear is shown here. Organ of Corti shows postmortem autolysis; however, hair cells are present (long arrows). As spiral ligament shrinks, radial dimension of cochlear duct becomes elongated and shallow. Spiral prominence and part of stria vascularis assume same plane as basilar membrane. Double arrow marks position of basilar crest, which is normal area of attachment of basilar membrane to spiral ligament. D-F) Atrophy of spiral ligament in 63-year-old woman who had not complained of deafness. Both cochleae show severe atrophy of spiral ligaments in middle and apical turns. Three views are shown from upper middle turn of left cochlea. D) Spiral ligament shows inner acellular zone and outer cellular zone (x107). At interface of these zones there is increase in density of fibrocytes. Stria vascularis is atrophied; however, this pathologic change bears no relationship to spiral ligament atrophy. E) In area adjacent to D, rupture has occurred in lateral wall of cochlear duct between basilar membrane and spiral prominence, creating confluence of endolymphatic space with acellular zone of spiral ligament (x119). F) Slightly more apicalward, stria vascularis has retracted outward and is attached to outer cellular zone of spiral ligament (x73). Organ of Corti in this ear shows postmortem autolysis but retains hair cells. It is not known what effect, if any, this pathologic change in spiral ligament might have on hearing. Certainly, these atrophic changes are pathologic, but it cannot be determined with certainty whether rupture is pathologic event or preparation artifact caused by shrinking effect of fixative solutions on already fragile spiral ligament.

the spiral ligament. In assessing morphologic changes of this magnitude, it is important to consider the possible role of postmortem autolysis and preparation artifact as contributors to these changes (Fig 9).

Atrophy of Reissner's membrane as a condition of aging has been described by Johnsson[54] and by Watanuki et al.[55] It is characterized histologically by vacuoles and blebs in the epithelial cell layer, thin-

ning of the membrane as a consequence of loss of cells, and irregularity in the distribution of both the epithelial and mesothelial cell layers. Rupture of Reissner's membrane may result from these atrophic changes. The membrane may collapse and distort the cytoarchitecture of the organ of Corti and entrap the tectorial membrane. These changes can occur without imposing a loss of hair cells or neurons, but presumably would interfere with the motion mechanics of the organ of Corti.

DISCUSSION

The findings of this study show that the basic tenet of four pathologic types of presbycusis is valid. It is apparent, however, that many aging ears show combinations of pathologic types. Whereas a particular type may predominate, its occurrence in total isolation from the others is the exception rather than the rule.

A loss of sensory cells appears to be the least important cause for hearing impairment caused by aging. The area of hair cell loss at the basal end of the cochlea may be a common cause for a threshold elevation for 8 kHz, but rarely does the degenerative change extend apicalward far enough to involve the speech frequencies. When a high-tone loss involves 4 kHz, it usually signals a lesion complicated by acoustic trauma.

The most consistent pathologic change in the aging cochlea is a loss of cochlear neurons. That the neurons that remain retain their dendritic fibers indicates that the missing neuronal units had undergone total degeneration, including dendritic fiber, soma, and axon — a condition termed primary neuronal degeneration. When a partial loss of neurons occurs as a secondary effect of atrophy of the organ of Corti, many (and often most) of the remaining neurons have lost their dendritic fibers — a condition termed retrograde or secondary neuronal degeneration. The only occasion in which retrograde neuronal degeneration occurs as a function of aging is severe sensory presbycusis, in which atrophy of the supporting cells of the organ of Corti causes injury to the dendritic nerve fibers. In this case the neuronal loss does not aggravate the hearing loss, because it is masked by the dominating sensory lesion.

Primary neuronal degeneration has to be in the range of a 90% loss to have an effect on pure tone thresholds — a condition also noted in animal studies.[56] Neuronal losses appear to have their greatest effect in degrading the capability for word discrimination; however, losses of up to 50% are compatible with normal or only slightly reduced word discrimination scores.

Atrophy of the stria vascularis, when it occurs as an effect of aging, is located principally in the apical half of the cochlea. It has a patchy distribution, and all cell layers are degenerated in the involved areas. The audiometric patterns show a strong tendency toward flat pure tone thresholds. We suspect that some biochemical or energy-providing function of endolymph is affected by strial degeneration, which causes a functional deficit throughout the endolymph of the cochlear duct, resulting in flat audiometric patterns.

In spite of every attempt to establish meaningful relationships between the cochlear disorders and corresponding audiometric abnormalities, including invoking the concept of a cochlear conductive lesion, there are about 25% of hearing losses of aging, mostly with flat audiograms, that cannot be explained by light microscopic study.

CONCLUSIONS

1. Sensory cell losses are the least important cause of hearing loss in the aged. The losses are located in the basal end of the cochlea and cause abrupt high-tone hearing losses; however, the lesions are often merged with acoustic trauma lesions and cannot be clinically or histologically differentiated from them.

2. Neuronal losses are a constant and predictable expression of the aging cochlea; however, in some cases the losses exceed the norm for age, thereby further degrading the capability for word discrimination.

3. Atrophy of the stria vascularis occurring as a predominant lesion of the aging cochlea is located principally in the apical and middle turns and characteristically is associated with hearing losses showing flat audiometric patterns.

4. Light microscopic studies have failed to reveal a pathologic correlate to explain the gradual descending pure tone threshold, and a cochlear conductive disorder seems the most logical explanation.

5. Many aging ears show significant involvement of two or more of the four basic pathologic types of presbycusis. The types appear to be additive, resulting in a wide spectrum of alterations in pure tone thresholds and word discrimination scores.

6. There is an indeterminate group consisting of about 25% of cases that do not meet the criteria for any of the four types of presbycusis, and it is assumed that the cause lies in morphological, chemical, and/or physical alterations that cannot be identified by light microscopic study.

7. The effectiveness of amplification for presbycusis depends in great part on the functional status of

these several cochlear structures. Their pathologic condition will determine pure tone threshold elevation, threshold gradients of the auditory spectrum, and word discrimination ability. Successful hearing aid design for presbycusis depends on providing comfortable amplification and control of background noise, but it is limited by pathophysiologic cochlear deficits that degrade stimulus coding. In the current state of medical knowledge, the degenerative changes of the aging cochlea are unyielding to medical therapy.

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